Urticaria & Angioedema

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Urticaria/Angioedema

- Occurs in 15-26 % of the population
- In acquired forms:
  - 50% have both types
  - 40% have urticaria only
  - 10% have angioedema only

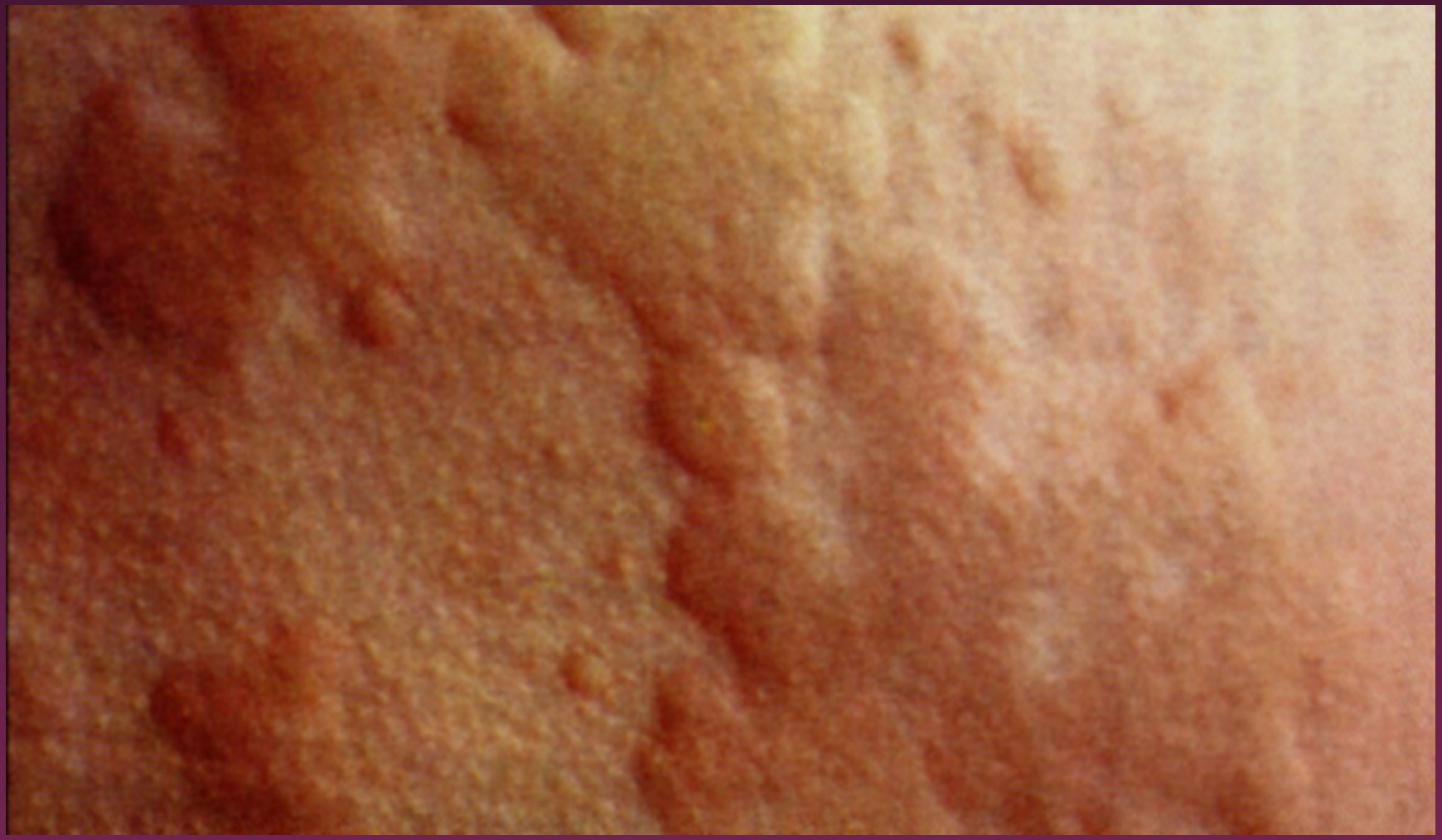
Natural History

- Urticaria alone:
  - 50% of patients with urticaria are free of lesions within 1 year
  - 20% continue to experience episodes for more than 20 years
- When angioedema accompanies urticaria:
  - 75% have symptoms for more than 1 year
  - 20% have have lesions more than 20 years

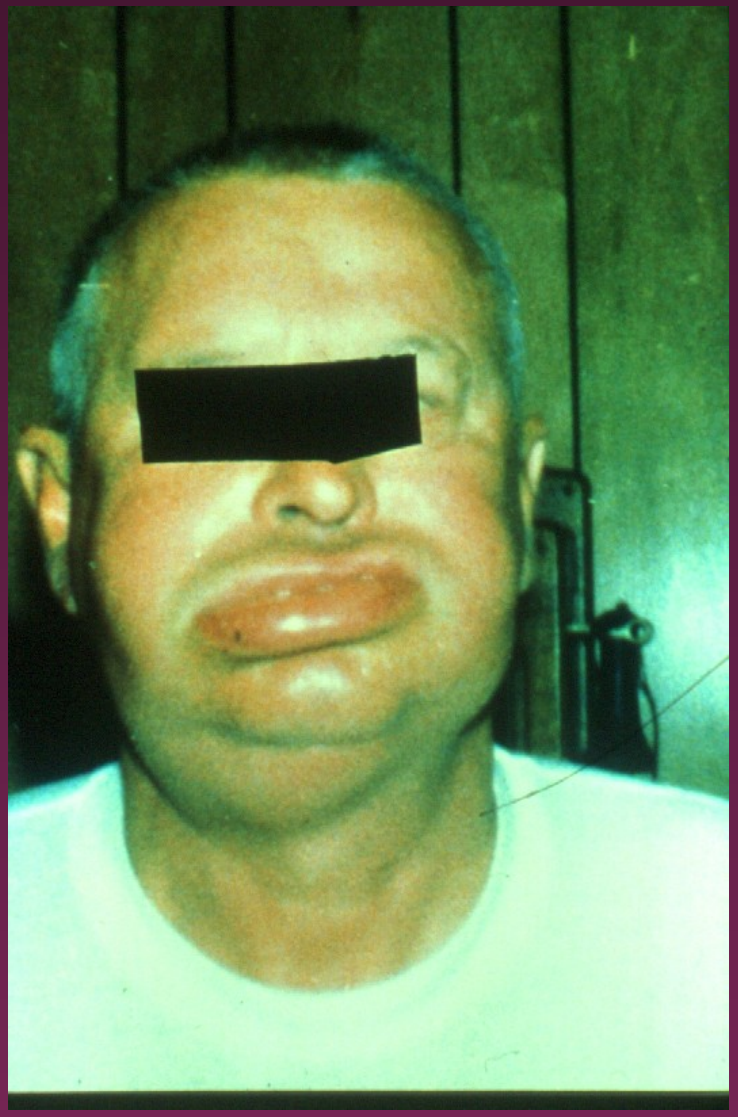
Clinical Appearance

- Urticaria
  - Raised, erythematous, blanchable, circumscribed area of edema involving the superficial dermis
  - Usually pruritic
  - Transient < 24 hours
- Angioedema
  - Extension of edema into deep dermis or subcutaneous and submucosal layers
  - Especially face (lips & periorbital area), tongue, hands, feet, pharynx
  - May persist several days

Urticaria



Angioedema



Urticaria/Angioedema Classification

- Acute
  - < 6 weeks duration
- Chronic
  - > 6 weeks duration
  - Idiopathic – as much as 70%
  - Autoimmune
  - Urticarial vasculitis

Some Potential Causes of Urticaria

- Medications
- Foods/Food additives
- Infections
- Insect bites and stings
- Contactants and inhalants
- Physical agents
  - Heat
  - Cold
  - Light
  - Pressure
  - Vibration
  - Water
  - Exercise
- Diseases
  - Collagen Vascular Disease - e.g. SLE, RA
  - Vasculitis
  - Serum sickness
  - Cryoglobulinemia
  - Endocrine disorders - hypo or hyper -thyroid, DM, progesterone hypersensitivity
  - Neoplasms
  - Mastocytosis

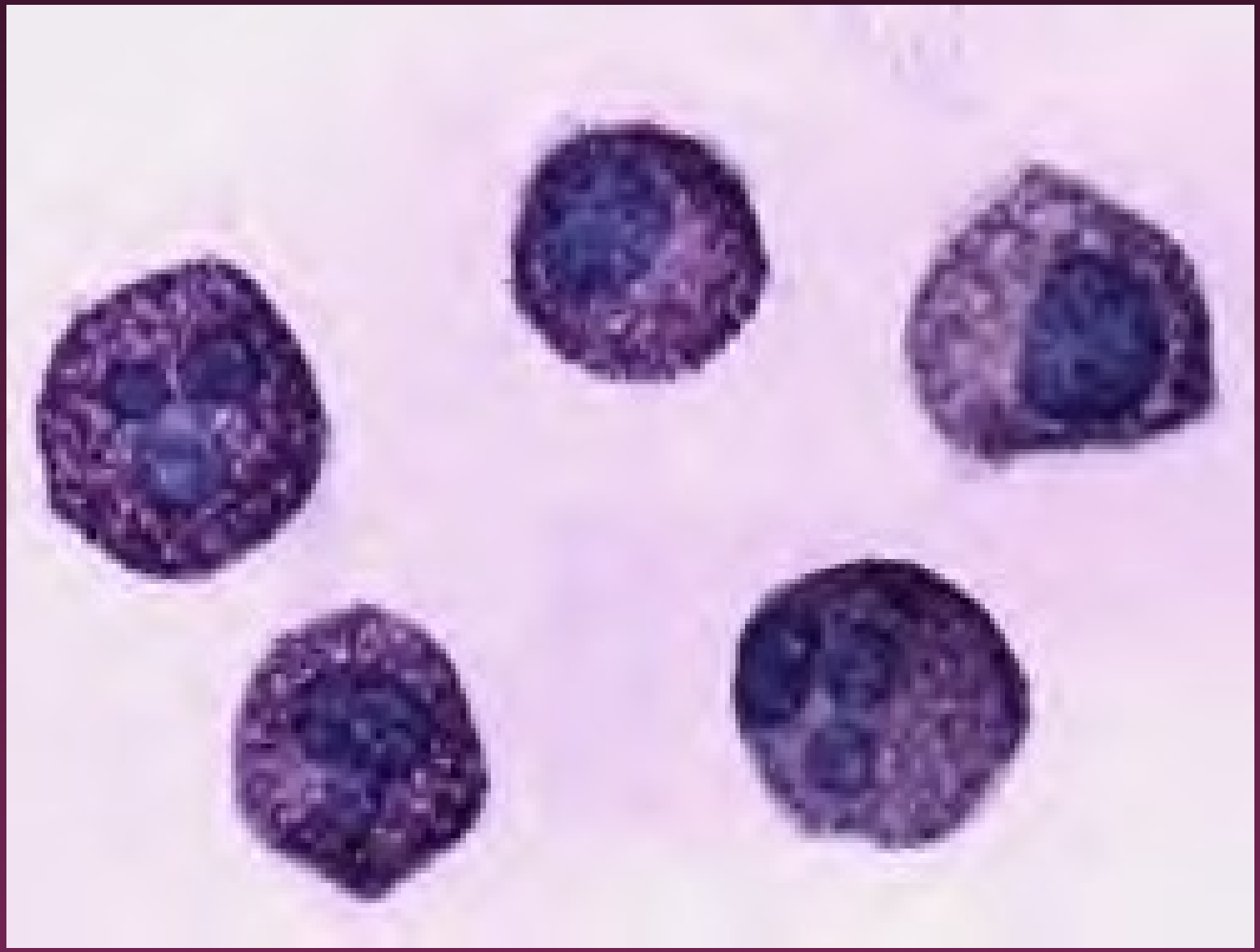
Differential Diagnosis

Urticaria

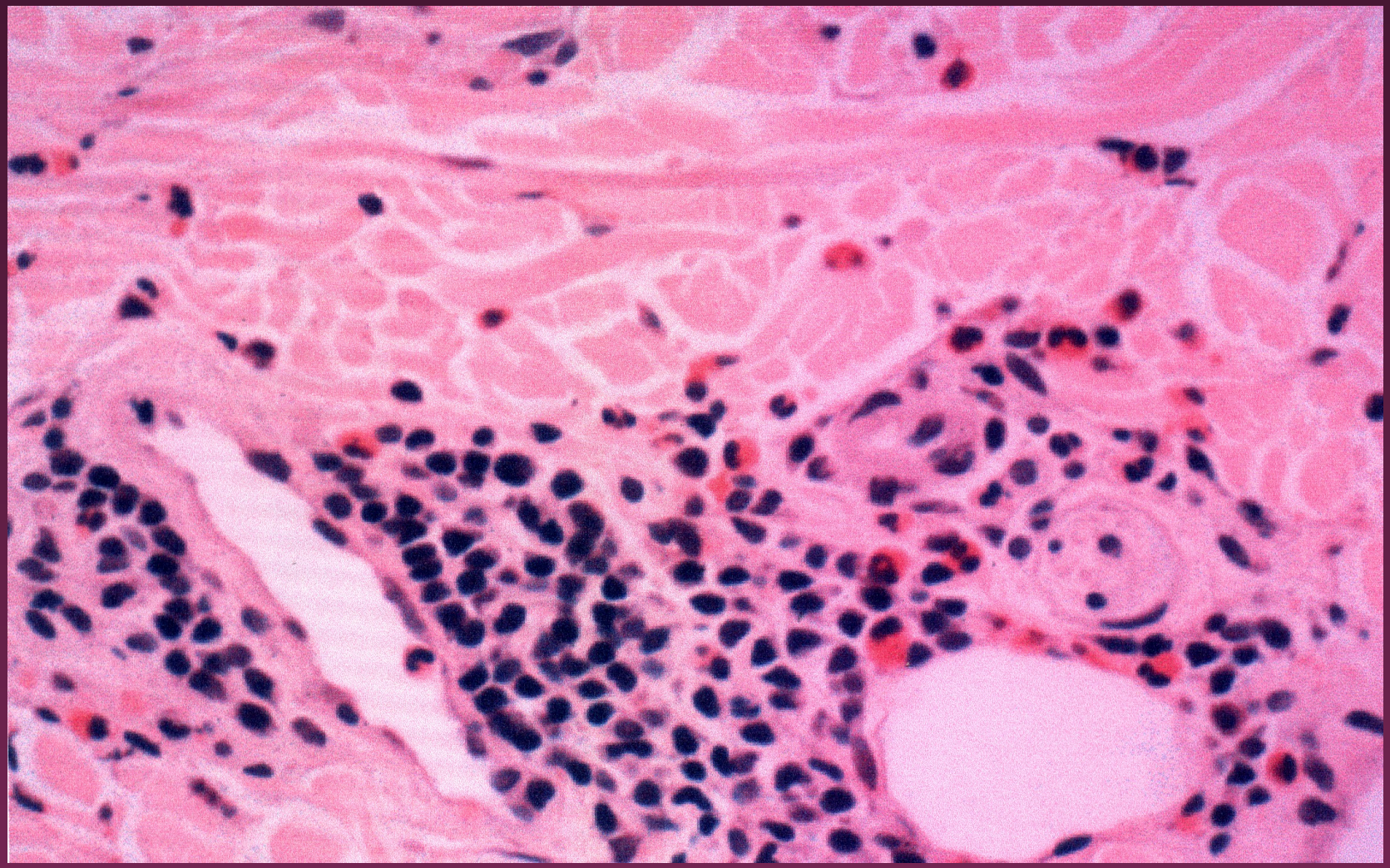
- Insect bites (papular urticaria)
- Erythema multiforme
- Bullous pemphigoid (urticarial stage)
- Urticaria pigmentosa
- Vasculitis and polyarteritis
- Systemic Lupus Erythematosus
- Morbilliform drug eruptions
- Dermatitis herpetiformis

Angioedema

- Anaphylaxis
- Melkersson-Rosenthal syndrome
- Erysipelas
- Cellulitis
- Contact dermatitis
- Photodermatitis



Urticaria



History: Acute Urticaria

- If acute think:
  - Drugs
  - Foods
  - Physical triggers
  - Infection exposures
  - Occupational exposures
  - Insect stings or bites

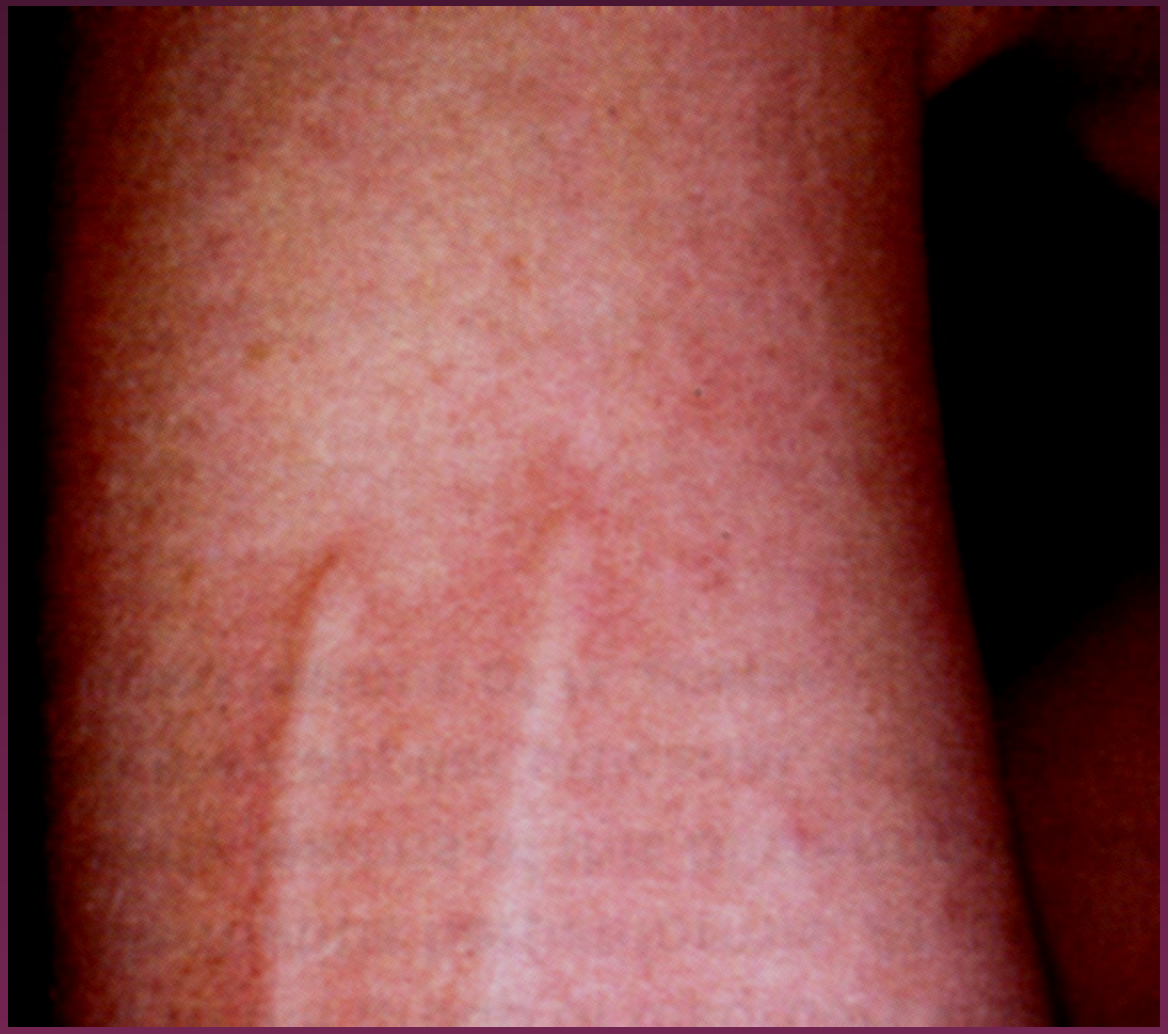
History: Chronic Urticaria

- Review of symptoms to assess
  - Infections
  - Collagen vascular disease
  - Malignancy

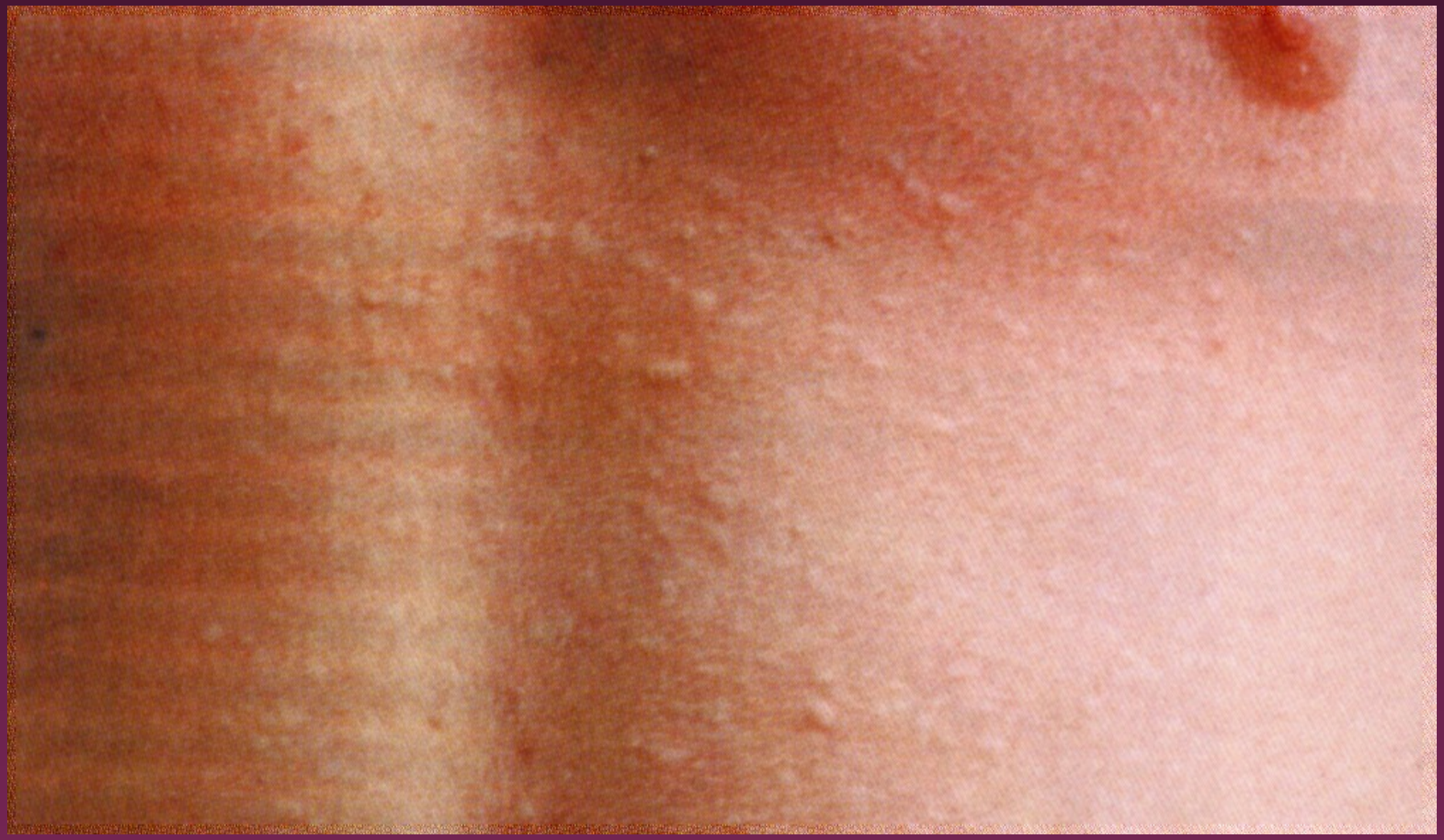
Physical Examination

- Appearance of skin lesions
  - Size
  - Depth
  - Pattern
  - Location
  - Features of UP, UV
- General PE looking for serious underlying illnesses

Dermographism



Cholinergic Urticaria



Physical Urticaria Evaluation

Type of Urticaria	Test
Dermographism	Stroke back
Cold	Ice cube
Cholinergic	Exercise, methacholine
Delayed pressure	Sand bag (wait >3 hour)
Solar	Phototest
Aquagenic	Water compresses
Vibratory angioedema	Vibratory mixer

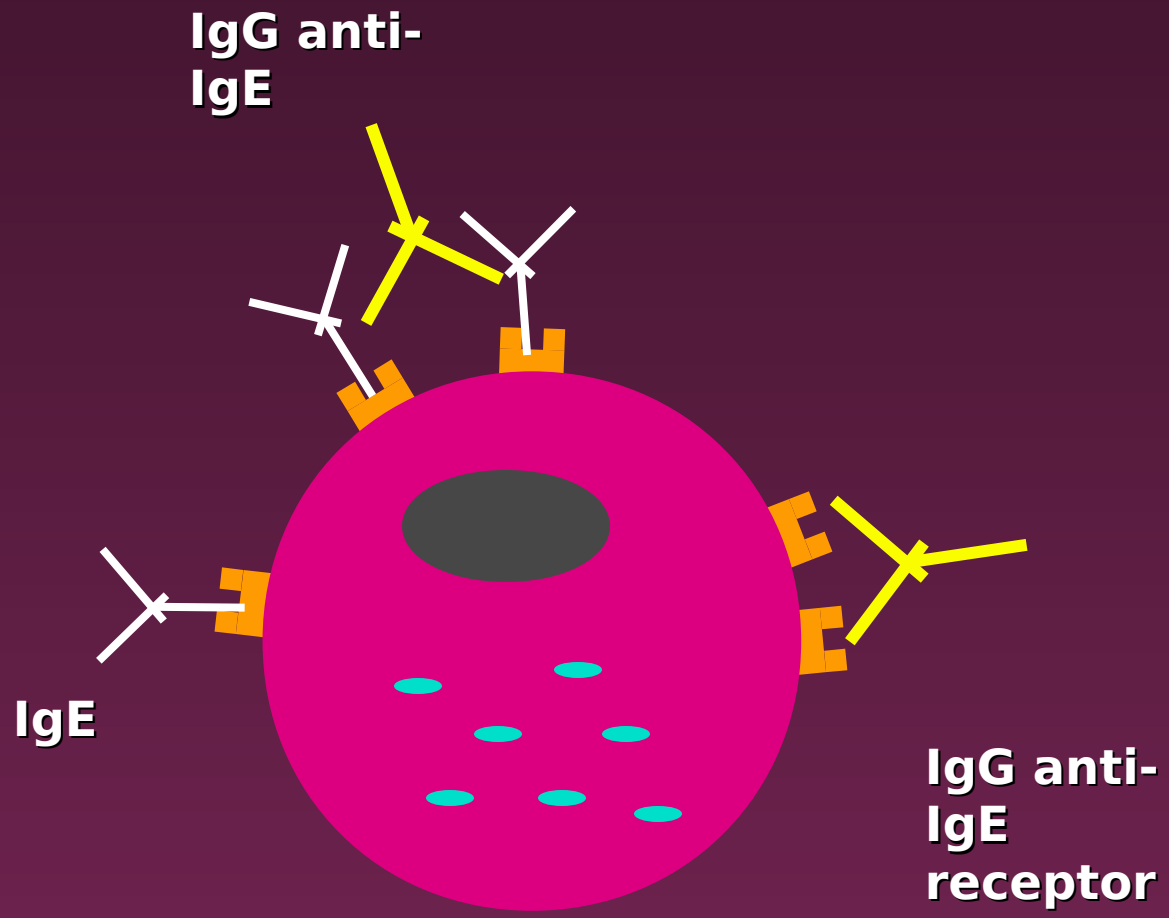
Work-up of Urticaria
How much?

- Most urticaria spontaneously clears within a few weeks
- Hence extensive workup not prudent until after 6 weeks duration
- At least 70% of urticaria, the cause is unknown - chronic idiopathic urticaria
- No consensus on number of labs but the diagnostic yield is usually low
- Labs should be directed by history and physical
- Skin testing not useful except perhaps in food allergy

Laboratory

- Consider
  - CBC
  - ESR
  - Liver panel
  - UA

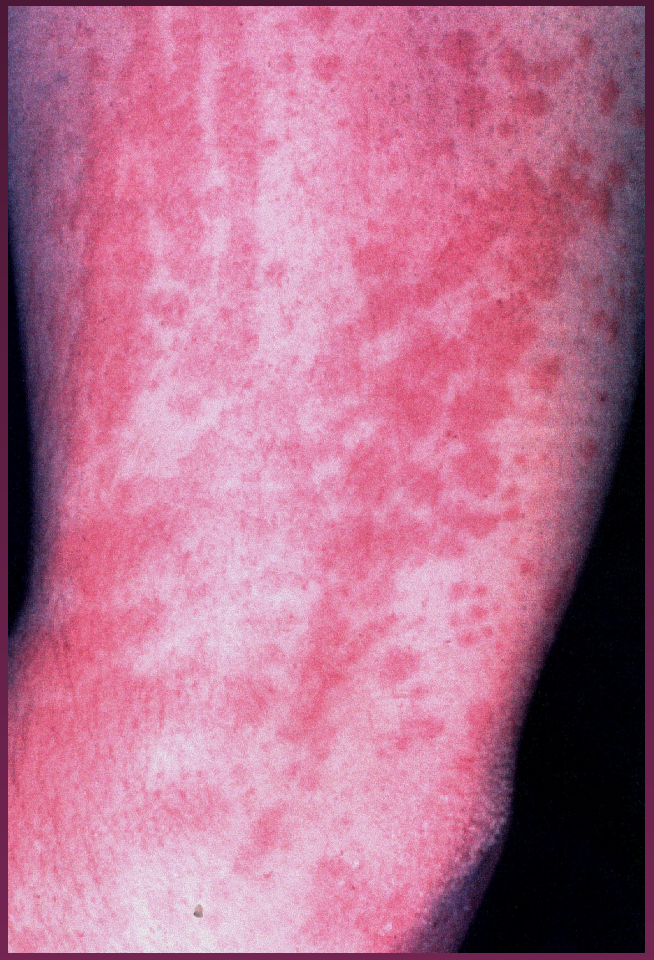
Autoantibodies and Chronic Urticaria



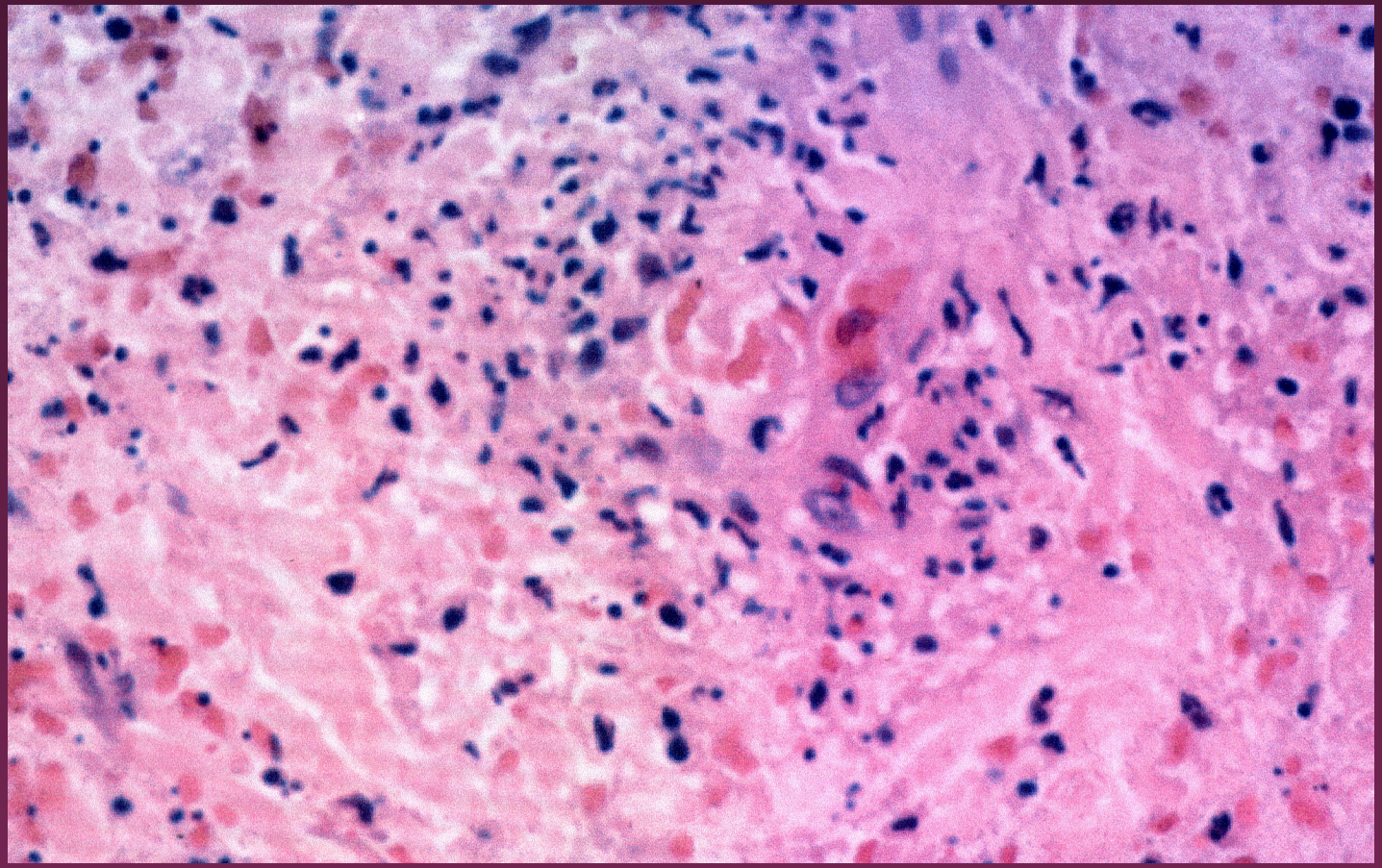
Urticaria
When to Biopsy

- Consider biopsy to r/o urticarial vasculitis or lesions
  - » Lesions lasting longer than 24 hours
  - » Lesions that are more prominent on the lower extremity than the trunk or arms
  - » Lesions with a purpuric component to them
  - » Lesions that leave stippling of hemosiderin pigment in wake of their healing
  - » Lesions associated with constitutional symptoms
  - » Urticaria that does not respond to conventional therapies

Urticarial Vasculitis



Histology of Urticarial Vasculitis

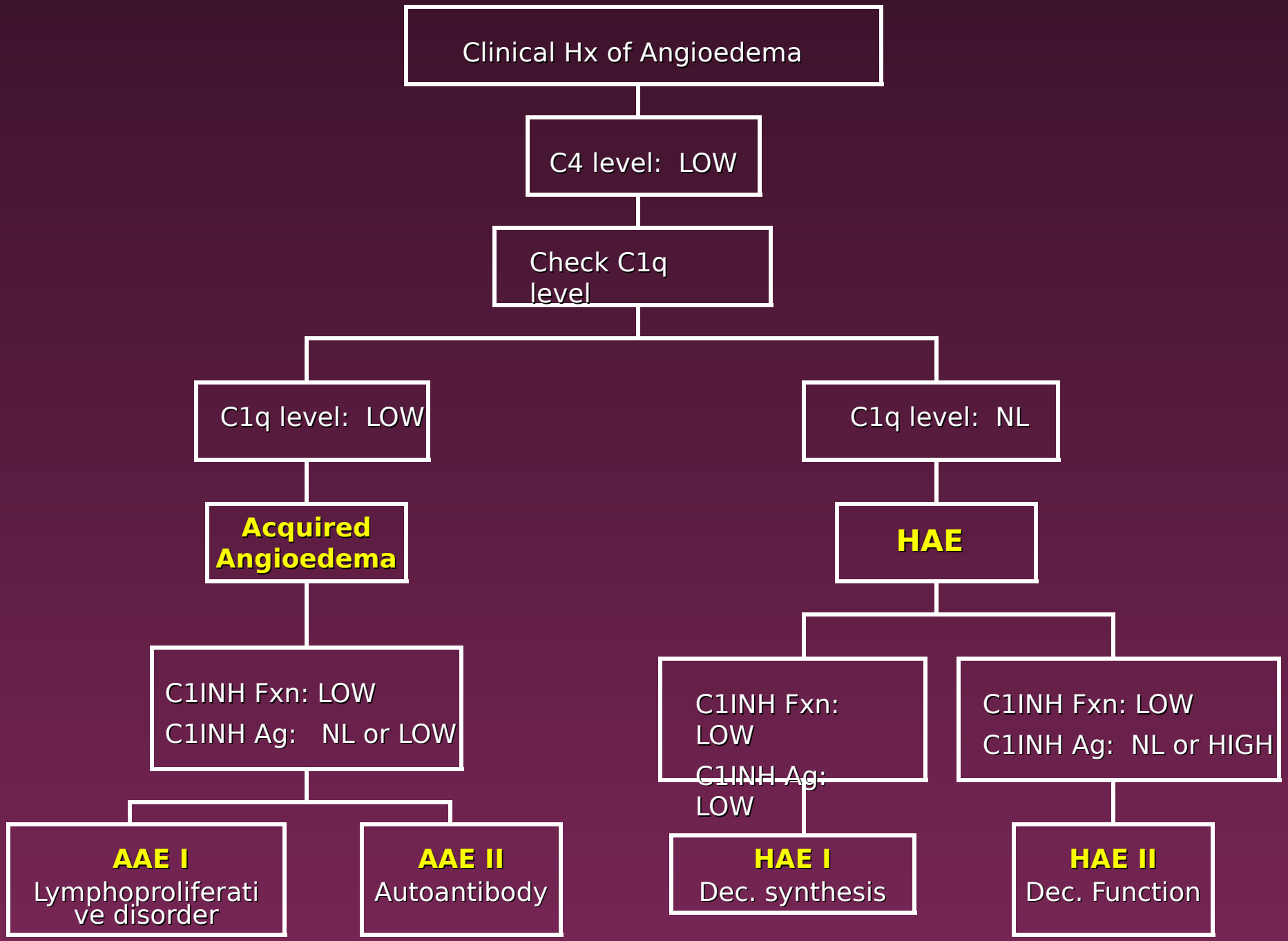


Angioedema: Spectrum of C1INH Deficiency

- Hereditary Angioedema (HAE)
  - » Impaired synthesis (type 1)
  - » Dysfunctional proteins (type 2)
- Acquired C1 INH deficiency (AAE)
  - » Type I: associated with
    - – B-cell lymphoproliferative disorders
    - – Connective tissue diseases
    - – Certain monoclonal gammopathies
  - » Type II: associated with autoantibody to C1 esterase inhibitor

Angioedema: Clinical Presentation of C1INH Deficiency

- Recurrent, circumscribed, nonpitting, subepithelial edema
- Usually affects extremities
- Urticaria is absent
- Concurrent or isolated visceral involvement--severe abdominal pain followed by watery diarrhea
- Attacks crescendo over several hours and may last several days
- May be precipitated by trauma, surgical procedures
- Mortality as high as 25% from laryngeal edema


Clinical Hx of Angioedema
C4 level: LOW
Check C1q level
C1q level: LOW
C1q level: NL
Acquired Angioedema
HAE
C1INH Fxn: LOW
C1INH Ag: NL or LOW
C1INH Fxn: LOW
C1INH Ag: LOW
C1INH Fxn: LOW
C1INH Ag: NL or HIGH
AAE I
Lymphoproliferative disorder
AAE II
Autoantibody
HAE I
Dec. synthesis
HAE II
Dec. Function

Angioedema: Therapy for HAE

- Acute Therapy is supportive
  - » maintain airway, tracheostomy, FFP?, Epi?
  - » Vapor-heated C1INH concentrate
- Preventative Therapy
  - » Attenuated androgens (danazol or stanozol)
    - – stimulate synthesis of C1INH by normal gene
    - – Contraindicated in children, growing adolescents and pregnant women

Angioedema: Drug Induced

- IgE hypersensitivity - e.g. Penicillin
- Cyclooxygenase inhibitors - NSAID’s, ASA
- Angiotensin Converting enzyme inhibitors
  - » Angioedema in 0.1 to 0.2% of treated patients
  - » Can occur after weeks/months of therapy
  - » Can take weeks after discontinuation to resolve

Urticaria & Angioedema Approach to Management

- Identification and removal of precipitating cause
- Administration of H1 receptor antagonist
- Administration of H1 and H2 receptor antagonists
- Combinations of H1 receptor antagonists
- Consider Doxepin
- Rare use of systemic corticosteroids for intractable episodes; attempt at alternate-day regimen
- Other therapies

Oral Steroids

- Use of steroids is warranted:
  - In severe cases of acute or chronic urticaria to achieve rapid relief
  - In refractory cases where H1, H2 and alternative agents have been unsuccessful
  - In the treatment of vasculitis
  - Topical steroids have no role

Additional Specific Therapies

- In some types of urticaria, specific therapies shown to be efficacious include:
  - Cold-induced urticaria - cyproheptadine
  - Pressure induced urticaria - steroids, NSAIDs
  - Leukocytoclasitic vasculitis - steroids; dapsone has been shown to be effective

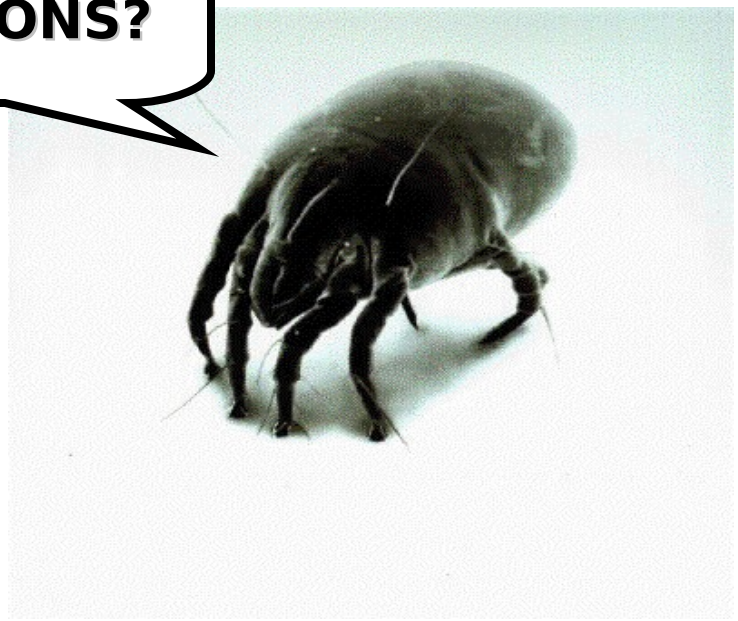
Other Therapies

- Oral beta agonists - may inhibit histamine release
- Calcium channel blockers - may interfere with mast cell activity
- Cetirizine - H1-blocker that has inhibitory effect on eosinophil migration
- Topical corticosteroids, topical antihistamines, and local anesthetics have no role in chronic urticaria
- Epinephrine indicated when laryngeal edema or evidence of anaphylaxis

Summary

- Acute urticaria- think food, drugs
- Chronic urticaria- history, physical exam, lab work-up directed at possible associated diseases
- Most chronic urticaria is idiopathic
- Skin test not useful except if food suspected as cause
- Antihistamines are mainstay of therapy
- Consider biopsy especially if UV suspected
- Check for C1 inhibitor deficiency in patients with angioedema without urticaria

QUESTIONS?



Dermatophagoides farinae
1000x